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**Provocative challenge to radiocontrast**

7/14/2010

**Q.** I have a 61 year old female with severe coronary artery disease who has a non-IgE mediated anaphylactic reaction (hypotension, respiratory distress) to radiocontrast media even with pretreatment with prednisone, diphenhydramine and ranitidine. Cardiologist would like to do a heart cath with stent placement but wants my advice on managing her RCM reaction. I have searched literature and concluded to recommend pre cath prep (prednisone, H1, H2 antihistamines), iso-osmolar RCM iodixanol (Visipaque) and IV graded challenge/desensitization to iodixanol. My question is: What is your recommended IV graded challenge/desensitization protocol? Thank you.

**A.** Thank you for your recent inquiry.

Your approach to this patient is correct. It is true that there are published graded challenge protocols for the administration of radiocontrast to a previous reactor. I am aware of two such protocols. The abstracts of the articles describing the protocols are noted below.

Unfortunately I could not gain access to the articles themselves because they were published so long ago. They would have to be ordered from your medical library. I would suggest, should you plan to do this procedure, that you use one of the two published protocols, gaining access to them via the medical library at your hospital. This would be the ideal way to proceed should you plan to do a graded challenge.

I have not used a graded challenge since the first publication of a pretreatment protocol in the 70's. If, however, you cannot gain access to the articles noted below, you could do a graded challenge utilizing serial dilutions of radiocontrast in saline. I would begin with a 1:1,000 dilution at an initial dose of 0.2 cc's. I would double the dose every 10 minutes, progressing through the 1:100, 1:10, and finally, the full strength preparation. Ten minutes after you have administered 1 cc of the full strength, you could proceed with the desirable dose of radiocontrast.

However, since this protocol has not been published, once again, it would be advisable for you to utilize one of the published regimens as noted in the abstracts.

Finally, a word of caution. On occasion, acute respiratory tract distress syndrome (shock lung) can be confused with an anaphylactic reaction (see Borish et al below). There are several cases in the literature of acute respiratory tract distress syndrome due to the administration of radiocontrast which reoccurred when radiocontrast was administered using pretreatment protocols. Characteristically this syndrome does not respond to a pretreatment regimen. You should do your best to determine whether or not your patient experienced an acute respiratory tract distress reaction rather than an anaphylactic reaction, because to my knowledge, pretreatment is not effective in preventing this reaction, and the graded challenge procedure has not been studied in such patients.

Thank you again for your inquiry and we hope this response is helpful to you.

Acta Radiol Diagn (Stockh). 1983;24(3):235-9.

Desensitisation as a means of preventing untoward reactions to ionic contrast media.

Agardh CD, Arner B, Ekholm S, Boijesen E.

Abstract

Patients with a previous history of anaphylactic reactions to ionic iodinated contrast media were desensitised before a second radiologic examination was performed. The tolerance to the contrast medium was raised by repeated intravenous injections in increasing doses and concentrations. No serious side effects were noted when the examinations with contrast medium was repeated within a few days after the desensitisation. The positive effect of the desensitisation may depend on a successive consumption of complement proteins, probably responsible for the allergic reactions. Therefore, the available amount of complement for some days may be too low for the occurrence of a complement reaction

J Allergy Clin Immunol. 1978 Nov;62(5):309-13.

Efficacy of intravenous pretesting and antihistamine prophylaxis in radiocontrast media--sensitive patients.

Yocum MW, Heller AM, Abels RI.

Abstract

Intravenous pretesting with radiocontrast media (RCM) was performed in 204 RCM-sensitive patients considered for repeat contrast radiography. Group 1 had vague histories of prior anaphylactoid reaction and negative pretests, and 2 of 41 (4.9%) had reactions upon contrast radiography. Groups 2 to 5 had definite histories of prior anaphylactoid reaction. Group 2 had the radiographic study cancelled: 18 of 21 (85.7%) had positive pretests. Group 3 had positive pretests and underwent contrast radiography, and 9 of 15 (60%) had reactions despite premedication. Group 4 (no premedication) and group 5 (diphenhydramine premedication) had negative pretests, but 11 of 53 (20.7%) and 3 of 71 (4.2%), respectively, developed reactions ( $p$  less than 0.001). The reaction frequency in group 3 (positive pretest) of 12 of 18 (66.7%) was greater than that in groups 4 and 5 (negative pretest) combined (14 of 124 (11.3%),  $p$  less than 0.001). Intravenous pretesting identified a high-risk group and diphenhydramine premedication decreased the frequency of reaction in patients sensitive to radiocontrast media.

J Allergy Clin Immunol. 1984 Jul;74(1):104-7.

Radiographic contrast media-induced noncardiogenic pulmonary edema: case report and review of the literature.

Borish L, Matloff SM, Findlay SR.

Abstract

Adverse reactions are a frequent complication of exposure to radiographic contrast media (RCM). These reactions are most often anaphylactoid in nature and are characterized by the occurrence of urticaria, angioedema, bronchospasm, and shock. In patients who have had an anaphylactoid reaction to RCM and in whom reexposure is indicated, various pretreatment protocols have been developed to mitigate the risk for recurrence. We report the case of a 46-year-old man who, while undergoing cardiac catheterization, developed noncardiogenic pulmonary edema. This is the first reported case of the occurrence of noncardiogenic pulmonary edema secondary to RCM documented with Swan-Ganz data. In addition, our patient developed noncardiogenic pulmonary edema despite pretreatment with prednisone and diphenhydramine, administered because of a past history of a similar reaction. Potential mechanisms for such a reaction are discussed.

Sincerely,

Phil Lieberman, M.D.

Key Words: radiocontrast media, anaphylaxis, oral challenge

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**Radiocontrast media reaction**

8/12/2004

**Q.** I am a neurologist and I recently ordered an angiogram on a patient with reported allergy to iodine (although not anaphylaxis). She did receive Benedryl prior to the procedure. Approximately 15 minutes after the angiogram was completed, she developed new onset weakness of the left arm and leg/ right facial weakness and tongue heaviness. I thought the symptoms were from a brainstem tia/vasospasm and treated them appropriately. Over the next 5 days she had some fluctuation in the neurological symptoms and severity including some subjective right sided weakness. All imaging including serial diffusion and spect MRI were negative. Hypotension was not an issue. Are there any reported immediate or delayed allergic reactions to iodine that can result in neurological dysfunction?

**A.** I do not know the nature of clinical manifestations diagnosed as "iodine allergy" in your patient. However, iodine sensitivity has nothing to do with the occasional adverse reactions to intra-vascular injections of radiocontrast media (RCM). Indeed, there is little, if any, convincing evidence that adverse reactions to RCM are immunologically mediated at all. However, despite a fair amount investigation, the exact mechanisms underlying most RCM reactions are still not well defined. Some reactions appear to be due to transient marked increases in blood osmolarity/viscosity. The latter could have conceivably caused transient obstruction of a small vessel in the brainstem possibly complicated by associated vasospasm. One would likely not see any vascular abnormality during imaging investigation obtained days after the reaction. Pre-treatment with an antihistamine such as Benadryl would not be expected to prevent such reactions. Of note, such RCM-induced osmolarity problems appear to be more common during rapid infusion of sizable amounts of the RCM and less common with the use of non-ionic RCM agents. A question may arise about the possible performance of RCM studies in this patient in the future, if absolutely necessary and unavoidable. There are no guarantees about not having an adverse reaction to the RCM (explained to the patient with written informed consent obtained). However, I think that these steps may reduce the risk:

- 1) Adequate hydration at the time of the RCM infusion
- 2) Use of a non-ionic RCM agent
- 3) Infuse as little RCM agent as feasible to get the desired image and at a slow rate
- 4) Consider pre-procedure use of low-dose heparin (similar to dosing for venous thrombosis prophylaxis)

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**Reaction to radiocontrast media**

2/2/2004

**Q.** **A patient states that they have had a past iodine reaction. Probably with the ionic dye. Is it ok to inject the patient with non-ionic iodine or are they at risk for an allergy again?**

**A.** I think that the reaction you are referring to is an adverse reaction to an intravascular injection of a radiocontrast media (RCM). Such reactions have nothing to do with the iodine content of the RCM. There is also no convincing evidence that they are truly allergic reactions. Since you did not describe the clinical manifestations in the reported previous reaction, my responses about RCM reactions will have to be general:

1) The incidence of most types of RCM adverse reactions are definitely less frequent when using the non-ionic RCM agents than with use of the older ionic RCM agents. However, very occasionally individuals with past histories of RCM reactions will react to injection of non-ionic RCM agents.

2) If the previous RCM reaction was just flushing, paresthesias but no objective signs of hypotension, respiratory difficulties, etc, one can usually avoid reactions by injecting the RCM at a slower infusion rate.

3) If the previous reaction was an anaphylactoid type (angioedema, wheezing, mild hypotension), the incidence of a similar repeat reaction to a RCM injection can be reduced considerably (though not completely eliminated) by a pre-treatment program using:

a) Oral prednisone 50 mg each at 12 hours, 6 hours, and 30 minutes prior to the RCM injection. Then steroids can be stopped at this point without further tapering of the dosage.

b) IM injection of diphenhydramine (Benadryl) 50 mg at 30 minutes prior to the RCM injection.

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